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Effectiveness of inactivated COVID-19 vaccines against severe illness in B.1.617.2 (Delta) variant-infected patients in Jiangsu, China

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Highlights

- The largest study of inactive COVID19 vaccine in preventing severe illness in China.
- Received two doses of inactivated vaccine had an 88% reduced risk in severe illness.
- The full immunization offered 100% protection from a severe illness among women.
- The effect of the vaccine was potentially affected by underlying medical conditions.

Abstract

Background The SARS-CoV-2 B.1.617.2 (Delta) variant has caused a new surge in the number of COVID-19 cases. The effectiveness of inactivated vaccines against this variant is not fully understood.

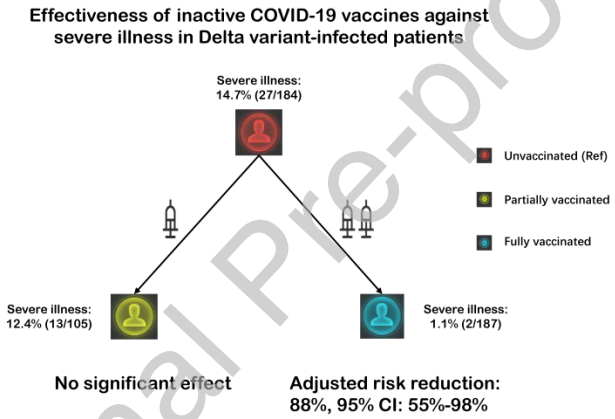
Methods Using data from a recent large-scale outbreak of B.1.617.2 SARS-COV-2 infection in Jiangsu, China, we conducted a real-world study to explore the effect of inactivated vaccine immunization on the course of disease in patients infected with the Delta variant.

Results Out of 476 patients with B.1.617.2 infection, 184 were unvaccinated, 105 were partially vaccinated, and 187 were fully vaccinated. Forty-two (8.8%) patients developed severe illness, of which 27 (14.7%), 13 (12.4%), and 2 (1.1%) were unvaccinated, partially vaccinated, and fully vaccinated, respectively (P <0.001). All 15 (3.2%) patients who required mechanical ventilation were unvaccinated. After adjusting for age, sex, and comorbidities, fully vaccinated patients had an 88%

reduced risk of progressing to severe illness ($OR_{adjusted}$: 0.12, 95% CI: 0.02-0.45). However, this protective effect was not observed in partially vaccinated patients ($OR_{adjusted}$: 1.11, 95% CI: 0.51-2.36). Full immunization offered 100% protection from severe illness among women. The effect of the vaccine was potentially affected by underlying medical conditions ($OR_{adjusted}$: 0.26, 95% CI: 0.03-1.23).

Conclusion Full vaccination with inactivated vaccines is highly effective at preventing severe illness in Delta variant-infected patients. However, partial vaccination does not offer clinically meaningful protection against severe disease.

Graphical abstract



Keywords

COVID-19; SARS-CoV-2; Delta variant; vaccine; effectiveness; severe illness

Introduction

According to the World Health Organization (WHO) estimation, as of January 5, 2022, the global cumulative number of confirmed COVID-19 cases has risen to over 293 million, and more than 5.4 million people have died from it (WHO 2021). There is no doubt that vaccination is a vital measure to contain the COVID-19 pandemic. Different COVID-19 vaccines, including inactivated, adenovirus vector, and mRNA

vaccines, have been authorized or are in the laboratory development and clinical utility evaluation stage (Folegatti et al. 2020, Jara et al. 2021, Kandeil et al. 2021, Polack et al. 2020). As of August 5, 2022, over 9.1 billion doses of the COVID-19 vaccines have been administered globally (WHO 2021). These vaccines can effectively induce immune responses against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (Sadarangani et al. 2021, Xia et al. 2021, Zhang et al. 2021). Clinical trials outside China demonstrated that vaccine efficacy for preventing symptomatic COVID-19 ranged from 65.9% to 83%, and severe illness or ICU admission ranged from 90% to 100% (Al Kaabi et al. 2021, Jara et al. 2021, Tanriover et al. 2021). In China, people are generally vaccinated with inactivated vaccines. Accumulated evidence suggests that an inactivated COVID-19 vaccine could efficiently, although not wholly, protect against SARS-CoV-2 infection and, more importantly, prevent severe illness progression. However, it is difficult to confirm in mainland China because there was no large-scale local outbreak after the first epidemic wave in 2020. Moreover, the protective effect of the inactivated vaccine on the pathogenesis of SARS-CoV-2 mutant strains is not clear.

On July 20, 2021, nine domestic COVID-19 cases were first identified through regular screening at the Nanjing Lukou International Airport, China (Polack et al. 2020). The outbreak at the airport spread rapidly to the surrounding areas, leading to outbreaks in Nanjing, Yangzhou, and Zhangjiajie. Genome sequencing confirmed that the etiologic agent was the SARS-CoV-2 B.1.617.2 (Delta) variant, which was first identified in Maharashtra, India, in late 2020 and now has spread globally (Voysey et al. 2021). Compared with the original type of SARS-CoV-2, the Delta variant has significantly increased virulence and transmissibility (Burki 2021, Liu et al. 2021, Zhang et al. 2021). Furthermore, the protective effect of vaccines against Delta variant

infection is weakened in many studies (Chen et al. 2021, Christensen et al. 2021, Lopez Bernal et al. 2021, Nasreen et al. 2021, Sheikh et al. 2021).

In the case of more than 200 million doses of COVID-19 vaccine administered in China, whether the widely used inactivated vaccine is still effective for the Delta variant is a question worthy of discussion. Thus, we performed a real-world study using patients' clinical and epidemiological data in a designated hospital in Nanjing. They were all linked to the outbreak of COVID-19 at the Nanjing Lukou International Airport. Our study aimed to describe to what extent the inactivated vaccine could prevent COVID-19 from progressing to severe illness in patients infected with the SARS-CoV-2 Delta variant.

Methods

Study design and population

We recruited 476 patients with confirmed COVID-19 treated in the isolation wards of Nanjing Public Health Medical Center from July to August 2021. The inclusion criteria were patients 1) aged over 18 years, 2) confirmed by SARS-CoV-2 nucleic acid PCR test, 3) linked to the recent outbreak of COVID-19 originating in Nanjing Lukou International Airport, and 4) infected with the Delta variant. China has adopted a dynamic zero-COVID policy. With this strategy, the surveillance system could efficiently track all the related cases whenever there was a local outbreak of COVID-19. In our study, samples from patients with COVID-19 were sequenced by the local Centers for Disease Control and Prevention if the SARS-COV-2 PCR cycle threshold (Ct) value was less than 30. All subjects were confirmed to have an epidemiological link with the sequencing-confirmed cases infected with the Delta variant.

The Nanjing Public Health Medical Center is the only designated hospital that provides medical services for COVID-19 patients in Nanjing. Of the 476 patients recruited in this study, 189 lived in Nanjing, 273 lived in Yangzhou, 12 lived in Huaian, and 2 lived in Suqian. We collected data from each patient, including demographic characteristics, medical history, vaccine status, comorbidities, clinical features, laboratory tests, treatments, and outcomes. The onset date was defined as when symptoms first appeared, or asymptomatic patients were detected for the first time with SARS-CoV-2 nucleic acid positivity. The diagnosis of severe illness was based on the "Guideline of COVID-19 Diagnosis and Treatment (trial version 8)" issued by the National Health Council of China. This study was approved by the ethics committee of Nanjing Public Health Medical Center (2020-LS-ky003). Written informed consent was waived by the Ethics Commission.

Vaccination status

Information regarding the time of vaccination and the type of vaccine was obtained from the electronic health information system. The time interval between the last dose of vaccination and the onset of disease was calculated. Because two weeks after the second dose were needed to develop protective immune responses against SARS-CoV-2 infection, a vaccine shot was considered effective only when the time interval between the second shot and disease onset was at least 14 days. We categorized patients into three groups: unvaccinated, partially vaccinated, and fully vaccinated according to immunization history. Patients were also considered unvaccinated if they had received one dose, but the time interval between the first shot and illness onset was less than 14 days. Likewise, patients who had received two vaccine shots for whom the time interval between the second shot and illness onset was less than 14 days were considered partially vaccinated (Figure 1)(Li et al. 2021).

Outcomes

The primary outcome of interest was the progression to severe illness in patients infected with the Delta variant. As defined by the "Guideline of COVID-19 Diagnosis and Treatment (trial version 8)" in China, severe illness of COVID-19 for adult patients must meet one of the following criteria: 1) respiratory rate ≥30 breaths/min, 2) oxygen saturation measured by finger pulse oximeter during air inhalation is ≤93% while at rest, 3) arterial partial pressure of oxygen (PaO_2)/oxygen uptake concentration (FiO_2) ≤300 mmHg, and 4) aggravated clinical symptoms and pulmonary imaging showing that the lesion progressed more than 50% within 24-48 hours. Patients with critical COVID-19 were those who had developed respiratory failure requiring mechanical ventilation or had evidence of shock or other organ dysfunction that needed transfer to the intensive care unit (ICU). The most severe condition of the patients during hospitalization was recorded. In this study, we analyzed severe and critical cases together.

Covariates

Covariates that have been confirmed in or possibly have a role in disease progression were considered, including age, sex, comorbidities, vaccination status, baseline SARS-CoV-2 viral load, and therapies (corticosteroids, intravenous immunoglobulin, and aerosol interferon-a). Age was categorized into two groups: 18-59 years and ≥60 years. Clinical parameters such as blood lymphocyte counts, C-reactive protein (CRP), interleukin-6 (IL-6), D-dimer, lactate dehydrogenase (LDH), and pulmonary involvement were more appropriate as an index of disease severity rather than risk factors and were therefore not included in the multivariable regression analysis. All cases involved in this study were vaccinated with the inactivated vaccine.

Statistical analysis

Categorized variables were expressed as frequencies, and continuous variables were described as medians (interquartile ranges, IQRs). As appropriate, comparisons were made using the Kruskal–Wallis test, Mann–Whitney U test, chi-square test, or Fisher's exact test. Factors related to severe illness were analyzed by univariate and multivariate regression analysis, and the relationship was expressed with odds ratios (ORs) and 95% confidence intervals (95% CIs). We also performed a subgroup analysis by stratifying age, sex, and underlying medical conditions. The significance level was set at 0.05. All analyses were performed using R software for Windows version 4.0.5 (https://www.r-project.org/).

Results

Characteristics of the patients

A total of 476 hospitalized patients were included in the analysis, of which 184 (38.6%), 105 (22.1%), and 187 (39.3%) were unvaccinated, partially vaccinated and fully vaccinated, respectively. The inactivated vaccines used were from CoronaVac (Sinovac Biotech, Beijing, China), BBIBP-CorV (Sinopharm, Beijing, China), and KCONVAC (BioKangtai, Shenzhen, China), accounting for 73.3%, 26.5%, and 0.2% of the vaccination shots, respectively. As shown in Table 1, although sex and C-reactive protein levels were similar among patients with different vaccination statuses, most of the variables were significantly different. Compared with unvaccinated patients, fully vaccinated patients were younger, less likely to have underlying illness, and had lower levels of interleukin-6 and lactate dehydrogenase. There was no statistical significance of the viral load between unvaccinated and fully vaccinated patients, either represented by the PCR Ct value of the ORF1ab gene (P=0.441) or the N gene (P=0.265).

Estimating the efficacy of inactivated SARS-CoV-2 vaccine

Forty-two (8.8%) patients developed severe illness, of which 27 (14.7%), 13 (12.4%), and 2 (1.1%) were unvaccinated, partially vaccinated, and fully vaccinated, respectively (*P* <0.001; Table 1). Fifteen (3.2%) patients required mechanical ventilation, all of whom were unvaccinated. The characteristics of the individuals categorized by severity of the disease are shown in Supplemental Table 1. As predefined in the methods, patients who had received one dose of vaccine and had acquired Delta variant infection within 14 days were deemed unvaccinated. This 14-day elapsed time was also applicable to the second dose vaccination. There was no significant difference in the proportion of severe illness between patients who did not receive any COVID-19 vaccine and patients who received one dose within 14 days (15.6% vs. 12.2%, *P* =0.750) or between patients who did not receive any COVID-19 vaccine and patients who received the 2nd dose within 14 days (12.8% vs. 11.1%, *P* =1.000). Therefore, our estimation of the effectiveness of vaccines would not be significantly biased by the definition of vaccination status.

Compared with the unvaccinated group, the fully vaccinated group had a significantly decreased risk of severe illness (OR: 0.06, 95% CI: 0.01-0.21, *P* <0.001; risk reduction: 94%, 95% CI: 79%-99%). The risk of severe illness was also decreased for the partially vaccinated patients, but the difference was not significant (OR: 0.82, 95% CI: 0.39-1.64, *P* =0.588) (Table 2). After adjusting for potential confounders, such as sex, age, and underlying medical conditions, the protective effect of full vaccination remained significant ($OR_{adjusted}$: 0.12, 95% CI: 0.02-0.45, *P* =0.006; adjusted risk reduction: 88%, 95% CI: 55%-98%). No significant effect was found for partial vaccination ($OR_{adjusted}$: 1.11, 95% CI: 0.51-2.36, *P* =0.783) (Table 2).

Subgroup analysis

The risk of progressing to severe illness was 0 in fully vaccinated persons without underlying medical conditions, age ≥60 years or female sex. Only 14 elderly patients were fully vaccinated, so the protection may be overestimated in this subgroup. The protective effect against severe illness remained significant for 18- to 59-year-old fully vaccinated persons ($OR_{adjusted}$: 0.12, 95% CI: 0.02-0.61, *P* =0.016; risk reduction: 88%, 95% CI: 39%-98%) and male fully vaccinated persons ($OR_{adjusted}$: 0.19, 95% CI: 0.03-0.86, *P* =0.049; risk reduction: 81%, 95% CI: 14%-97%). The effect of the vaccine was potentially affected by underlying medical conditions, resulting in the reduced protective effect of full vaccination ($OR_{adjusted}$: 0.26, 95% CI: 0.03-1.23). Partial vaccination had no significant protective effect on severe illness in any subgroup (*P* >0.05) (Table 3).

Discussion

Mutations of SARS-CoV-2 have attracted significant public attention, with variants of concern leading to increased transmissibility, impaired immune protection from the vaccine, more severe disease, or compromised diagnostic capacity (Khateeb et al. 2021). The Delta variant, which was first identified in India, is more transmissible than other lineages of SARS-CoV-2 and is now becoming the major strain driving the COVID-19 pandemic (Campbell et al. 2021, Singh et al. 2021, Vaughan 2021). Vaccine breakthrough caused by the Delta variant has been increasingly reported, even in massively vaccinated regions (Mizrahi et al. 2021, Vaughan 2021). Therefore, concern has been raised regarding whether herd immunity bolstered by inactivated vaccines in China could protect against the Delta variant.

In late May, the first attack by this new virus occurred in Guangzhou, China, with

approximately 160 cases involved (Lopez Bernal et al. 2021). A real-world study on 74 patients and 292 negative controls calculated that the overall effect for two-dose vaccination was 59.0% protective against SARS-CoV-2 infection and 100% protective against severe illness (Li et al. 2021). Our present study focusing on 476 hospitalized patients demonstrated that the risk of progression to severe illness substantially decreased in fully vaccinated patients. After adjusting for age, sex, and underlying medical conditions, the risk reduction remained significant at 88%. Moreover, in our study, inactivated vaccines provided 100% protection against mechanical ventilation. This is the largest real-world study to confirm the effectiveness of inactivated vaccines in preventing severe illness caused by the Delta variant in China.

It is well known that underlying comorbidities and old age are risk factors for severe illness in SARS-CoV-2-infected patients(Jordan et al. 2020). This is consistent with findings from our study. Severe illness did not occur in fully vaccinated patients without underlying medical conditions (100% protection). Both fully vaccinated patients who developed severe illness had underlying diseases. Interestingly, 100% protection was also found in elderly patients who had been fully vaccinated. Since only 14 elderly patients were fully vaccinated, the protective effect of inactivated vaccines might be overestimated in this study. Fully vaccinated women were 100% protected against progression to severe illness, while fully vaccinated men had only a reduced risk of 81%. Whether sex disparities exist in COVID-19 vaccine efficacy needs to be further explored.

Although an entire course of vaccination could efficiently protect COVID-19 patients from progressing to severe illness, the protective effect could not be identified in partially vaccinated patients. This may be due to a relatively high viral burden and

decreased immune protection in Delta variant-infected patients (Christensen et al. 2021, Lopez Bernal et al. 2021, Nasreen et al. 2021). The baseline viral load in this study, as represented by the Ct value of the real-time quantitative reverse transcription polymerase chain reaction (RT–PCR), was 20 (IQR: 16-25), which is much higher than that (median: 30; IQR: 25-34) in our previous data during the first outbreak of COVID-19 in 2020 (Hu et al. 2020). In the context of Delta variant infection, relatively higher immunity may be necessary, which generally would be achieved after full vaccination (Sadarangani et al. 2021). It is worth noting that in addition to personal protection and vaccination, enhancing the ability of countries or regions to respond to public health concerns is also crucial for COVID-19 control (Ji et al. 2021).

There are some limitations to our study. First, we confirmed the protective effect of inactivated vaccines in preventing the progression to severe illness, but we could not estimate vaccine efficacy against Delta variant infection because all participants were confirmed COVID-19 cases. Second, since individuals who have been protected from disease would not develop a severe illness related to COVID-19, the effectiveness of inactivated vaccines against severe disease in our study based on infected cases would be, to some extent, an underestimation of that based on the whole population.

In conclusion, we found that complete course immunization with inactivated vaccines could effectively protect against severe illness caused by the Delta variant in China. The protective effect is affected by underlying medical conditions. Partial vaccination does not offer clinically meaningful protection against severe illness. Our study highlights the importance of continuous efforts in encouraging a full course of vaccination.

NOTES:

Contributions

Jianming Wang, Peng Huang, and Yongxiang Yi conceived and designed the study. Yongxiang Yi, Zhiliang Hu, Yan Song, Changhua Yi, and Junwei Li contributed to the recruitment of participants. Jianming Wang, Zhiliang Hu, Peng Huang, Bilin Tao and Zhongqi Li led the data collection, data analysis and data interpretation. Zhiliang Hu, Bilin Tao and Zhongqi drafted the manuscript. All authors provided critical review and final approval of the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Declaration of interests

All authors have no conflict of interest to declare.

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Figure 1. Definition of Different Vaccination status

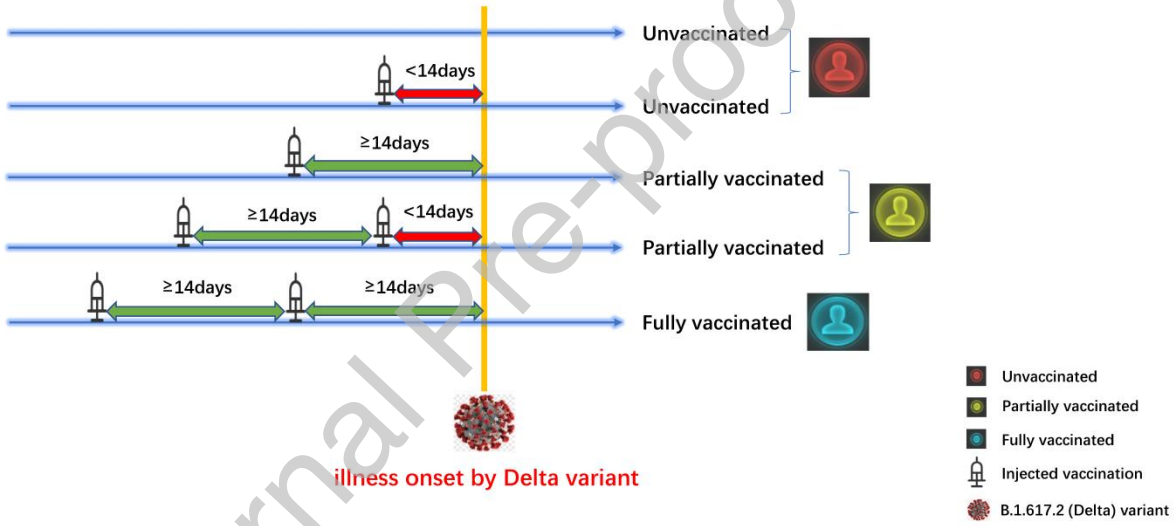

Figure 1 Defination of Different Vaccination status

Table 1. Baseline characteristics and disease outcome among 476 SARS-COV-2 Delta variant infected patients with different vaccination statuses.

Variables	**Unvaccinated (n=184)**	**Partially vaccinated (n=105)**	**Fully vaccinated (n=187)**	***P***
Gender				0.213
Female, n(%)	115 (62.5)	92 (53.3)	185 (63.1)	
Male, n(%)	69 (37.5)	49 (46.7)	69 (36.9)	
Age (years)				
18-59, n(%)	56 (30.4)	69 (65.7)	173 (92.5)	<0.001
≥60, n(%)	128 (69.6)	36 (34.3)	14 (7.5)	
Comorbidity	83 (45.1)	35 (33.7)	33 (17.6)	<0.001
Hypertension, n(%)	62 (33.7)	24 (23.1)	23 (12.3)	<0.001
Diabetes, n(%)	24 (13.0)	10 (9.6)	9 (4.8)	0.021
Heart disease, n(%)	14 (7.6)	5 (4.8)	2 (1.1)	0.005
Cancer, n(%)	7 (3.8)	3 (2.9)	1 (0.5)	0.074
COPD, n(%)	3 (1.6)	0 (0.0)	0 (0.0)	0.18
Asthma, n(%)	6 (3.3)	1 (1.0)	2 (1.1)	0.344
Autoimmune disease, n(%)	2 (1.1)	1 (1.0)	2 (1.1)	1
Time from illness onset to hospitalization, median(IRQ) days	3.0 (2.0, 5.0)	3.0 (1.0, 4.0)	2.0 (1.0, 4.0)	<0.001
Symptoms				
Fever, n(%)	75 (40.8)	38 (36.5)	51 (27.3)	0.021
Cough, n(%)	96 (52.2)	50 (48.1)	98 (52.4)	0.748
Shortness of breath, n(%)	13 (7.1)	7 (6.7)	3 (1.6)	0.020
Abdominal pain or diarrhea, n(%)	12 (6.5)	4 (3.8)	12 (6.4)	0.635
Loss of smell or taste, n(%)	5 (2.7)	2 (1.9)	12 (6.4)	0.120
Stuffy nose or runny nose, n(%)	16 (8.7)	16 (15.2)	35 (18.7)	0.020
Pharyngeal discomfort, n(%)	33 (17.9)	27 (25.7)	43 (23.0)	0.257
Laboratory findings				
C-reactive protein, median (IRQ) mg/L	5.6 (1.8, 15.0)	7.8 (2.5-20.9)	5.7 (2.1, 14.3)	0.248
>10, n(%)	66 (35.9)	47 (44.8)	65 (34.8)	0.205

Interleukin-6, median (IRQ) pg/mL	18.3 (9.4, 32.5)	13.7 (4.9, 24.9)	6.1 (1.5, 13.6)	<0.001
>6.6, n(%)	153 (83.1)	31 (70.5)	89 (47.6)	<0.001
Neutrophil count, median (IRQ) $\times10^9$/L	2.9 (2.0, 3.6)	3.0 (2.3, 4.2)	3.2 (2.3, 4.2)	0.047
Lymphocyte count, median (IRQ) $\times10^9$/L	1.1 (0.8, 1.4)	1.3 (0.9, 1.7)	1.2 (0.9, 1.6)	0.004
<0.8, n(%)	40 (21.7)	17 (16.2)	29 (15.5)	0.252
LDH, median (IRQ) U/L	249.5 (214.8, 289.0)	240.0 (204.0, 286.0)	231.0 (199.0, 269.0)	0.007
>245, n(%)	95 (51.6)	49 (46.7)	75 (40.1)	0.083
ALT, median (IRQ) U/L	18.9 (13.8, 28.5)	20.7 (13.1, 32.1)	16.6 (11.4, 26.3)	0.024
>40, n(%)	25 (13.6)	16 (15.2)	23 (12.3)	0.777
Viral load (Ct value)				
ORF1ab gene, median (IRQ)	23.0 (20.0, 27.0)	25.0 (21.0, 29.0)	22.0 (19.0, 27.5)	0.016
N gene, median (IRQ)	20.0 (17.0, 24.0)	22.0 (18.0, 27.0)	20.0 (15.0, 24.0)	0.019
SARS-COV-2 antibody, S/CO				
IgM, median (IRQ)	0.07 (0.04, 0.36)	0.71 (0.15, 3.49)	0.34(0.11, 1.24)	<0.001
IgG, median (IRQ)	0.11(0.06, 0.37)	1.50 (0.2, 33.6)	5.49 (2.3, 35.0)	<0.001
Outcome				
Severe illness, n(%)	27(14.7)	13 (12.4)	2 (1.1)	<0.001
Mechanical ventilation, n(%)	15(8.2)	0 (0.0)	0 (0.0)	<0.001

Data were expressed as median (interquartile range, IQR) or n (%). Comparisons among groups were made using the Kruskal-Wallis test, Chi-Square test, or Fisher's exact test, as appropriate. The Ct value was used to represent the viral load. Abbreviation: COPD, chronic obstructive pulmonary disease; LDH, lactate dehydrogenase; ALT, alanine aminotransferase; Ct, cycle threshold; S/CO, signal to cut-off; SARS-COV-2, severe acute respiratory syndrome coronavirus 2.

Table 2 Univariable and multivariable analysis for factors associated with severe illness

Variables	Univariable model		Multivariable model	
	Crude OR (95% CI)	***P***	**Adjusted OR (95% CI)**	***P***
Sex				
Female	1		1	
Male	1.45 (0.76-2.75)	0.249	1.48 (0.76-2.87)	0.247
Age (years)				
18-59	1		1	
≥60	4.83 (2.46-10.07)	<0.001	2.37 (1.08-5.47)	0.036
Comorbidity				
No	1		1	
Yes	2.33 (1.23-4.43)	0.009	1.33 (0.67-2.65)	0.415
Vaccination status				
Unvaccinated	1		1	
Partially vaccinated	0.82 (0.39-1.64)	0.588	1.11 (0.51-2.36)	0.783
Fully vaccinated	0.06 (0.01-0.21)	<0.001	0.12 (0.02-0.45)	0.006
Time from illness onset to hospitalization (per day)	1.06 (0.94-1.17)	0.309	-	-
Ct value (N gene)	0.99 (0.94-1.04)	0.649	-	-

OR, odds ratio; CI, confidence interval; Ct, cycle threshold

Table 3. Effectiveness of inactivated COVID-19 vaccines against severe illness in patients infected with Delta variant

	Unvaccinated (Ref.)	Partially vaccinated				Fully vaccinated				
	N	N	OR (95%CI)	*P*	OR_{adj}(95%CI)	P_{adj}	N	OR (95%CI)	*P*	OR_{adj} (95%CI)	P_{adj}
All patients											
Non-Severe illness	157	92	1		1		185	1		1	
Severe illness	27	13	0.82 (0.39-1.64)	0.588	1.11 (0.51-2.36)	0.783	2	0.06 (0.01-0.21)	< 0.001	0.12 (0.02-0.45)	0.006
With underlying medical conditions											
Non-Severe illness	68	31	1		1		31	1		1	
Severe illness	15	4	0.59 (0.16-1.77)	0.374	0.54 (0.14-1.77)	0.341	2	0.29 (0.04-1.12)	0.117	0.26 (0.03-1.23)	0.121
Without underlying medical conditions											
Non-Severe illness	89	60	1		1		154	1		1	
Severe illness	12	9	1.11 (0.43-2.77)	0.821	1.83 (0.65-5.1)	0.247	0	0	-	0	-

			9)		0)						
18-59 years											
Non-Severe illness	51	64	1		1		171	1		1	-
Severe illness	5	5	0.80 (0.21-3.00)	0.731	0.67 (0.17-2.66)	0.562	2	0.12 (0.02-0.57)	0.013	0.12 (0.02-0.61)	0.016
≥60 years											
Non-Severe illness	106	28	1		1		14	1		1	-
Severe illness	22	8	1.38 (0.53-3.33)	0.491	1.37 (0.52-3.31)	0.502	0	0	-	0	-
Male											
Non-Severe illness	57	43	1		1		67	1		1	
Severe illness	12	6	0.66 (0.22-1.85)	0.446	0.80 (0.24-2.48)	0.702	2	0.14 (0.02-0.55)	0.013	0.19 (0.03-0.86)	0.049
Female											
Non-Severe illness	100	49	1		1		118	1		1	
Severe illness	15	7	0.95 (0.35-2.42)	0.921	1.37 (0.47-3.74)	0.545	0	0	-	0	-

OR, odds ratio; CI, confidence interval; OR_{adj}, adjusted odds ratio